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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,170	02/01/2002	Tse Wai-Choi Eric	109312.	9703
7590 09/10/2008				
Henry N Wixon Hale & Dorr Suite 1000 1455 Pennsylvania Avenue NW Washington, DC 20004			EXAMINER GABEL, GAILENE	
			ART UNIT 1641	PAPER NUMBER
			MAIL DATE 09/10/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/936,170	ERIC ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	GAILENE R. GABEL	1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 16 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1, 4, 5, 7-11 and 14-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 5, 7-11, and 14-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____.                                     |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____.   | 6) <input type="checkbox"/> Other: _____.                         |

## **DETAILED ACTION**

### ***Amendment Entry***

1. Applicant's amendment and response filed on May 16, 2008 is acknowledged and has been entered. Claim 1 has been amended. Claim 18 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Currently, claims 1, 4, 5, 7-11, and 14-18 are pending. Claims 1, 4, 5, 7-11, and 14-17 are under examination.

### ***Withdrawn Rejections***

2. All rejections and objections not reiterated herein, have been withdrawn.
3. In light of Applicant's amendment, the rejection of claims 1, 4, 5, 7-11, and 14-17 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.
4. In light of Applicant's amendment and arguments, the rejection of claims 1, 4, 5, 7-11, and 14-17 under 35 U.S.C. 112, first paragraph, is hereby, withdrawn.

### **New Grounds of Rejection**

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 4, 5, 7-11, and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gargano et al. (From Phage Libraries to Intracellular Immunization, Intracellular Antibodies: Development and Applications (1997) Chapter 10, pages 174-186)).

Gargano et al. state that "if scFV fragments can be successfully expressed in a yeast two hybrid format, monitoring their [stable] interaction with a corresponding [target] antigen should allow isolation of those scFv fragments that bind successfully to the antigen under intracellular expression conditions" (p. 176, 2<sup>nd</sup> full ¶). In a subsequent experiment, Gargano et al. demonstrated that a positive interaction can be obtained between antigen-antibody pair in a two hybrid yeast format. Accordingly, Gargano et al. teach a method of determining efficient binding and positive interaction of an immunoglobulin (scFv) to a target in an intracellular environment, whereupon the immunoglobulin is expressed in a yeast two hybrid system, whereupon novel

immunoglobulins that bind successfully are caused to be isolated (Abstract, p. 176, 2<sup>nd</sup> full ¶ and Fig. 10.1 (A)). Gargano et al. specifically provide in page 173, first full paragraph that “the yeast two-hybrid system has been successfully used to directly assay interactions between known proteins to study protein interaction domains and to isolate novel interacting partners for a protein of interest.” In practice, a first fusion polypeptide comprising an immunoglobulin (scFv fragment) fused to a first molecule and a second fusion polypeptide comprising a target fused to a second molecule, are caused to be expressed in an intracellular environment whereupon the first and the second molecules are separable domains of a reporter molecule. In the yeast two hybrid system, activation of a reporter construct which produces a detectable reporter molecule, i.e. resulting to a stable interaction that generates a signal, occurs when the two domains are brought together through the binding interaction of the two polypeptides expressed as activation domain (VP16) and DNA binding domain (LexA) fusion proteins. Detection of a signal from the detectable reporter molecule provides indication of binding between the immunoglobulin and the target in an intracellular environment. The generation of a signal can be manifested by a change in optical property and monitored using colorimetric assay. Gargano et al. specifically teach that the level of reporter activation that generates a signal correlates well with specific binding of proteins which further gives an indication of the strength, i.e. stability, of the interaction (p. 174, 4<sup>th</sup> full ¶ to p. 176, 1<sup>st</sup> full ¶). The active reporter molecule may be an enzyme and the method is performed in the presence of a substrate (p. 177, 1<sup>st</sup> full ¶).

The immunoglobulins can be provided by immunoglobulin-encoding nucleic acids within mammalian cells, from phage libraries encoding a repertoire of immunoglobulins (p. 177, 2<sup>nd</sup> to 4<sup>th</sup> full ¶s). The libraries can be constructed from nucleic acids isolated from an organism which has been challenged by antigen (p. 180, 1<sup>st</sup> and 2<sup>nd</sup> full ¶). Gargano et al. teach selecting immunoglobulins and further subjecting them to functional intracellular assay (Fig. 10.2). Cells can be sorted (rescued) on the basis of phenotype conferred by the intracellular immunoglobulins.

Gargano et al. is silent in teaching that no prior application of a phage display is [necessarily] used to isolate immunoglobulins that bind to a target.

However, it is noted that each element and method steps necessary to determine binding of an immunoglobulin to a target in an intracellular environment as claimed, are specifically taught by Gargano et al. In as far as the recitation of "no prior application of a phage display is used to isolate immunoglobulins that bind to a target" Gargano apparently suggested such limitation in page 176, second full paragraph, in stating that "if scFv fragments can be successfully expressed in a yeast two hybrid format, monitoring their [stable] interaction with a corresponding [target] antigen should allow isolation of those scFv fragments that bind successfully to the antigen under intracellular expression conditions", and in demonstrating in a subsequent experiment that "a positive interaction can be obtained between antigen-antibody pair in a two hybrid yeast format" using method steps in the reference that are consonant to the claimed invention. It is, therefore, deemed that Gargano et al. renders obvious the claimed invention.

It is further maintained that the "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges and conditions by routine experimentation." Since Applicant has not disclosed that the specific limitation recited in claim 1, step a) which recites, "no prior application of a phage display is used to isolate immunoglobulins that bind to a target" is for any particular purpose or solve any stated problem and the prior art otherwise, teaches all the elements, structures, and functions that are recited in claim 1, absent unexpected results, it would have been obvious for one of ordinary skill to try to discover other optimum workable conditions of the methods disclosed by the prior art by normal optimization procedure.

### ***Remarks***

6. Applicant's arguments filed on May 16, 2008 are now moot in light of the new grounds of rejection.
7. No claims are allowed.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAIENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday to Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/  
Primary Examiner, Art Unit 1641

September 8, 2008